<u>We claim</u>:

1. A method for differentiating one or more pluripotent embryonic stem (ES) cells toward one or more neural cells comprising:
(a) culturing the ES cells at low density in the serum-free media; and
(b) allowing said ES cells to differentiate toward the neural cells.

2. The method faccording to claim 1 for differentiating embryonic stem cells to cells with markers characteristic of neural cells comprising:
(a) culturing the embryonic stem cells in a serum free media at low cell density wherein said density is selected to minimize ES cell aggregation or EB formation;
(b) allowing said cells to differentiate.

3. The method of claim 2 wherein the density is selected as to avoid EB formation.

4. The method of claim 1 wherein said cell density is greater than 0 cells/μl to 50 cells/μl.

5. The method of claim 4 wherein the cell density is greater than 0 cells/μl to 20 cells/μl.

6. The method of claim 5 wherein the cell density is greater than 0 cells/μl to 10 cells/μl.

7. The method of claim 6 wherein the cell density is 10 cells/μl.

8. The method of claims 6 wherein there is no EB formation.

9. The method of claim 7 wherein the differentiating ES cells form at least one neuro sphere.

10. The method of claim 1 wherein the differentiating ES cells form at least one neurosphere.

11. The method of claim 1 wherein the serum free media further comprises a cytokine.

12. The method of claim 11 wherein the cytokine is leukemia inhibitory factor (LIF).

13. The method of claim 12 wherein the ES cells differentiate into a primitive neural stem cell, that is pluripotent.

14. The method of claim 1 and 12 wherein the serum free media further comprises a growth factor.

15. The method of claim 14 wherein the growth factor is selected from the members of the fibroblast growth factor (FGF) family of growth factors.

16. The method of claim 15 wherein the growth factor is FGF2.

17. The method according to claim 1 wherein the media comprises an inhibitor of TGF-ß -related signaling.

18. The method of claim 17, wherein the inhibitor is the protein Noggin.

19. The method of claim 18 wherein the inhibitor is selected from the Cerebus family of proteins.

20. A method for producing secondary neural stem cell colonies comprising:

(a) culturing ES cells in low cell density completely defined

serum-free media for a time and under conditions sufficient to differentiate the said ES cells;

(b) dissociating and subcloning primary neural cell colonies generated from the said ES cells; and

(c) administering a growth factor to the dissociated neural cells.

21. A method according to claim 20 wherein the growth factor is selected from among the members of the fibroblast growth factor (FGF) family of growth factors.

22. A method according to claims 21 wherein the growth factor is FGF2.

23. A method according to claim 20 wherein a cytokine is administered to the dissociated neural cells.

24. A method according to claim 23 wherein the cytokine is LIF or B27.

25. One or more cell(s) expressing one or more neural precursor cell marker(s) and/or one or more neural-specific mRNA molecule(s), and having multilineage potential.

26. A cell according to claim 25 wherein the neural precursor marker nestin is expressed.

27. A cell according to claim 25 or 26 wherein the neural-specific mRNA molecule is Emx2 or HoxB1

28. A method according to anyone of claims 1 or 12 for analyzing the role of genes in the regulation of neural fate specification.

29. A primitive neural stem cell produced by the method of claims 12

that comprises neural cell markers and is pluripotent.

30. A primitive neural stem cell produced comprising at least one neural cell marker and is pluripotent

31. A method of producing a pre-selected cell type derived from a cell of claim 30 comprising, culturing the cells under differentiating conditions that promote formation of the cell type.

32. The method of claim 31 wherein the pre-selected cell type is a neural cell, and the differentiating conditions comprise culturing the cell in a serum free media that comprises FGF2.

33. A method for screening for modulators of cellular differentiation comprising,
(a) culturing pluripotent cells in serum-free media under low density conditions in the presence of the potential modulator;
(b)allowing for differentiation of the cells;
(c) detecting any differentiation of the cells and cell types generated, if any.

34. A method in accordance with claim 33 wherein the modulators comprise any culturing conditions that may modulate cellular differentiation.

35. A method for screening for differentiation factors of cellular development comprising :

(a) culturing the cells in serum free media at low cell density in the presence of the differentiation factor;
(b) allowing cells to differentiate;
(c) detecting differentiation of the cells, if any.

36. A method of claim 35 for screening for modulators or differentiation factors of neural cell development.

37 A method for screening for differentiation factors of cellular development comprising :

(a) culturing the cells of claim 29 in serum free media, in the present of the differentiation factor.
(b) detecting any differentiation of the cells.

38. The method of claim 37, wherein the media further comprises FGF2.

38. A modulator or differentiation factor detected by the methods of claims 33-37.

39. A method according to claim 38 for modulating cellular differentiation.

40. The method of claim 1 for obtaining a homogenous uniform cell base.

41. The method of claim 40 wherein the cell base is a neural cell base.

42. A method for supplying cells for transplantation comprising culturing cells pursuant to the method of claim 1 or 12.

43. A method for treating neurdegenerative disorders comprising administering to a patient in need thereof the cells of claim 29.

44. A method for the treatment of any disease or conditions resulting from cell loss or function in the neural system comrpising administering the cells of claim 29 to a patient in need thereof.

45. A method of gene thereapy, wherein the cell of claim 29 is modified to express a gene of interest and administering siad modified cell to a patient in need thereof.